REMARKS

As an initial matter, Applicants note with appreciation that the claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f) and receipt of the certified copies of the priority documents have been acknowledged in the present Office Action. The Examiner is also thanked for returning a signed and initialed copy of the Form PTO-1449 submitted in the Information Disclosure Statement filed December 17, 2001.

Reconsideration and withdrawal of the rejections made in the instant Office Action are respectfully requested, in view of the following remarks.

Summary of Specification Amendments

The Specification is amended to correct a typographical error in the term "*Gordonia*" which appears throughout the specification as suggested by the Examiner. No new matter is added.

The Specification is amended to include the recitation "in a culture broth" to more clearly define the present invention. No new matter is added.

Summary of Claim Amendments

Claims 1-9 are amended to more particularly claim the subject matter of the invention.

Clam 1 has been amended to include the recitation "in a culture" to more clearly define the claimed invention. Support for this amendment can be found throughout the specification, in particular at the bridging paragraph between pages 2 and 3, and the third full paragraph of page 3. Therefore, no new matter is added.

Claim 1 has been amended to remove the recitations "(herein referred to as compound (I-a))", "(herein referred to as compound (I-b))", "(herein referred to as compound (II-a))", "(herein referred to as compound (II-b))" to remove redundancies from the claim.

Claim 2 has been amended to remove the recitations "(herein referred to as compound (III-a))", "(herein referred to as compound (III-b))", "(herein referred to as compound (IV-a))", "(herein referred to as compound (IV-b))" to remove redundancies from the claim.

Claim 3 has been amended to remove the recitations "(herein referred to as compound (V-a))", "(herein referred to as compound (V-b))", "(herein referred to as compound (VI-a))", "(herein referred to as compound (VI-b))" to remove redundancies from the claim.

Claim 4 has been amended to remove the recitations "(herein referred to as compound (VII-a))", "(herein referred to as compound (VII-b))", "(herein referred to as compound (VIII-a))", "(herein referred to as compound (VIII-b))" to remove redundancies from the claim.

Claim 5 has been amended to remove the recitation "or treated cells" to remove redundancy from the claim as suggested by the Examiner.

Claims 6-8 are amended to correct a typographical errorin the term "*Gordonia*" which appears throughout the specification as suggested by the Examiner. Therefore, no new matter is added.

Claim 6 has been amended to include the recitation "and having no ability to sporulate and showing no hyphal growth in a culture" to more clearly define the claimed invention. Support for this amendment can be found throughout the specification, in particular at the bridging paragraph between pages 2 and 3, and the third full paragraph of page 3. Therefore, no new matter is added.

Claim 8 has been amended to replace the recitation "ATCC15098" with "IFO15098" to correct a typographical error. No new matter is added.

Claim 9 has been amended to replace recitation "*Gordona sp.* ATCC19067" with "*Rhodococcus rhodochrous, sp.* ATCC19067 to correct a typographical error. No new matter is added.

Summary of Office Action

(1) In the Office Action, the Examiner objects to the specification and suggests that the application be reviewed for errors. The Examiner points out, in particular, that the correct spelling of "*Gordona*" throughout the specification and claims should be "*Gordonia*".

(2) The Examiner rejects Claims 7-9 under 35 U.S.C. § 112, first and second paragraphs, as allegedly not being sufficiently enabled by the specification and/or failing to particularly point out and distinctly claim the invention. In this regard, the Examiner alleges that several of the ATCC numbers recited in the rejected claims do not correspond to the names of the species of bacteria that are recited in combination therewith in Claims 8 and 9.

(3) Claim 8 is rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which allegedly was not sufficiently described in the specification to be enabled thereby. In particular, the Examiner inquires about the designations "JCM", "IFM" and "IFO" recited in Claim 8 and requests a declaration to the effect that the corresponding strains were publicly available at the time of the invention.

(4) Claims 1-9 are rejected under 35 U.S.C. § 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the invention. In this regard, the Examiner notes that Claim 1 recites that the cultured microorganism does not show hyphal growth and alleges that in contrast, the genera, species and strains recited in Claims 6-9 which all depend from Claim 1, do show hyphal growth to at least some extent. In particular, the Examiner asserts that with one exception (*Shingomonas*), all of the genera recited in Claims 6-9 belong to the *Actinomycetes*, the latter being acknowledged at page 2, last paragraph, of the present application to "grow with filamentous forms by elongating hyphae". Additionally, the rejection alleges that the expression "treated cells" in Claim 5 is redundant.

(5) Claims 1-9 are rejected under 35 U.S.C. § 102(a), as allegedly anticipated by or, in the alternative, under 35 U.S.C. § 103(a), as allegedly obvious over each of four documents, i.e.:

(a) WO 99/60151 to Kranjc et al. (corresponding to U.S. Patent No. 6,365,382);

(b) U.S. Patent No. 6,043,064 to Davis et al. (corresponding to Japanese Application No. 7-184670 acknowledged at page 2 of the present application);

(c) U.S. Patent 5,942,423 to Demain et al.; and

(d) Okazaki et al., J. Antibiot. 36: 1176-1183, 1983.

Objections to the Specification

The Specification is amended to correct a typographical errorin the term "*Gordonia*" which appears throughout the specification as suggested by the Examiner. No new matter is added.

Rejection of Claims 7-9 under 35 U.S.C. § 112, first and second paragraphs

The Examiner rejects Claims 7-9 under 35 U.S.C. § 112, first and second paragraphs, as allegedly not being sufficiently enabled by the specification and/or failing to particularly point out and distinctly claim the invention. In this regard, the Examiner alleges that several of the ATCC numbers recited in the rejected claims do not correspond to the names of the species of bacteria that are recited in combination therewith in claims 8 and 9.

A. ATCC953, ATCC8363, and ATCC186

Applicants respectfully point out that ATCC953, ATCC8363 and ATCC186 have been reclassified as new species respectively after the filing of the present application.

(i) ATCC953

With regard to ATCC953 being recited as *Exiguobacterium acetylicum* in the ATCC catalogue, Applicants respectfully point out that the recitation "*Brevibacterium acetylicum*" in Claim 7 and the recitation "*Brevibacterium acetylicum* ATCC953" in

Claim 8 have been deleted. Therefore, the rejection directed to ATCC953 has been rendered moot.

(ii) ATCC8363

With regard to ATCC8363 being as *Desemzia incerta* in the ATCC catalogue, Applicants respectfully point out that the recitation "*Brevibacterium incertum*" in Claim 7 and the recitation "*Brevibacterium incertum* ATCC8363" in Claim 8 have been deleted. Therefore, the rejection directed to ATCC8363 has been rendered moot.

(iii) ATCC186

With regard to ATCC186 being recited as *Kocuria rosea* in the ATCC catalogue, Applicants respectfully point out that as shown on page 143 of Reference 1 (American Type Culture Collection, Fifteenth Edition, 1982 , a copy of which is attached herewith), ATCC186 was recited as *Micrococcus roseus* prior to the filing of this application. Thus, it appears ATCC186 has been reclassified as *Kocuria rosea.* Accordingly, Applicants respectfully point out that the recitation of *Micrococcus roseus* ATCC186 in Claim 8 is definite and enabled.

B. ATCC15098 and ATCC19067

Applicants respectfully submit that the recitations "ATCC15098" and "ATCC19067" recited in Original Claims 8 and 9 contain typographical errors. Applicants have amended Claims 8 and 9 to correct these typographical errors.

(i) ATCC15098

With regard to the recitation "ATCC15098", Applicants respectfully submit that this recitation contains a typographical error. This recitation has been replaced by the

recitation "IFO15098" in Amended Claim 8. Specifically, the recitation "*Sphingomonas terrae* ATCC15098" has been replaced with the recitation "*Sphingomonas terrae* IFO15098" in Amended Claim 8.

As shown in Reference 2 (ATCC website , a copy of which is attached herewith), ATCC15098 is recited as *Glomerella cingulata*. In contrast, IFO15098 is recited as *Sphingomonas terra* IFO15098. Due to a typographical error, Original Claim 8 recites "*Sphingomonas terra* ATCC15098" instead of "*Sphingomonas terra* IFO15098". The reason for this error is presented below.

As recited at lines 14-20 of page 3 of the present application, the present inventors have discovered that if hydroxylation of compound (V-a) or compound (V-b) can be carried out with a microorganism having hydroxylation activity, having no sporulability and showing no hyphal growth, disadvantages, such as reducing the reaction efficiency due to microorganism contamination caused by the release of spores during the production process or the heterogeneity of culture solution caused by formation of hyphae could be avoided. Hence, this would be industrially advantageous. The inventors of this application have finally discovered such microorganisms and invented the claimed invention. Filamentous fungi is a microorganism having sporulability and showing hyphal growth. ATCC15098 has been classified as *Glomerella cingulata*, namely filamentous fungi, prior to the filing of this application, as shown on page 380 of Reference 1 (Catalogue of Strains I, Fifteen Edition (1982) , a copy of which is attached herewith). Therefore, it is clear that Applicants have no motivation to evaluate the hydroxylation activity of ATCC15098 which is filamentous fungi.

Further, as shown in Reference 3 (Institute for Fermentation, Osaka (IFO), website , a copy of which is attached herewith), *Sphingomonas terrae* has been deposited as IFO15098 at Institute for Fermentation (IFO) which is an official organization for deposit of microorganisms.

As mentioned above, the recitation "*Sphingomonas terrae* ATCC15098" was erroneously recited in Original Claim 8, and has been replaced as "*Sphingomonas terrae* IFO15098" Amended Claim 8. This amendment is not a new matter, but a correction of simple typographical error. Thus, the rejection of ATCC15098 has been overcome by Amended Claim 8 replacing the recitation "ATCC15098" with "IFO15098".

(ii) ATCC19067

With regard to ATCC19067 being recited as *Rhodococcus rhodochrous sp.* in the ATCC catalogue; Applicants respectfully submit that the recitation "*Gordona sp.* ATCC19067" in Claim 8 has been replaced with "*Rhodococcus rhodochrous sp.*"

As shown at pages 182-183 of Reference 1 (Catalogue of Strains I, Fifteen Edition (1982)), ATCC19067 was recited as *Rhodococcus rhodochrous sp.* prior to the filing of the present application. The recitation "*Gordona sp.* ATCC19067" instead of "*Rhodococcus rhodochrous sp.* ATCC19067" recited in Original Claim 9 was a typographical error. Applicants respectfully submit that this typographical error had been corrected in the amendment of Claim 8, replacing "*Gordona sp.* ATCC19067" to *Rhodococcus rhodochrous sp.* ATCC19067. Applicants also respectfully submit that this amendment does not contain a new matter, but a correction of a simple error. Thus,

Applicants respectfully submit that the rejection of ATCC19067 has been overcome by Amended Claim 8.

C. ATCC21430, ATCC21387, ATCC19240, ATCC7005 and ATCC15921

With regard to the rejection directed to ATCC21430, ATCC21387, ATCC19240, ATCC7005 and ATCC15921, Applicants respectfully submit that the names of the species direct to ATCC21430, ATCC21387, ATCC19240, ATCC7005 and ATCC15921 in the ATCC catalogue are not correct. The names of the species direct to ATCC21430, ATCC21387, ATCC19240, ATCC7005 and ATCC15921 recited in this application are taxonomically correct and are definite and enabled for the reasons presented below.

(i) As to the fact that ATCC21430 is recited as Nocardia sp. in the ATCC catalogue

Applicants respectfully submit that as shown on page 159 of Reference 1 (Catalogue of Strains I, Fifteen Edition (1982)), ATCC21430 is classified as *Nocardia sp.,* a strain which was deposited by Kyowa Hakko Kogyo Co., Ltd who is an assignor of this application.

Applicants have classified ATCC21430 as *Nocardia sp.* at the time of deposit to ATCC, and examined again various chemotaxonomical characteristics of the strain prior to the filing of this application. As a result, it has been found that many chemotaxonomical characteristics of ATCC21430 are consistent with those of microorganisms belonging to *Rhodococcus*. For example, the main menaquinone of ATCC21430 is MK-8(H_2) as in microorganisms belonging to *Rhodococcus* (Page 2337

of Reference 4 (Bergey's Manual of Systematic Bacteriology, volume 4, 1989) , a copy of which is attached herewith)), while the main menaquinone of microorganisms belonging to *Nocardia sp.* is MK-8(H_4) or MK-9(H_2).

Applicants respectfully submit that when a DNA-DNA homology test was carried out for type strains of microorganisms belonging to *Rhodococcus*, ATCC21430 showed a high value of 75% with ATCC13808 which is a type strain of *Rhodococcus rhodochrous*. Generally, it is recognized that the homology value which can confirm the identity of the species between two strains in DNA-DNA homology test is around 70%. Therefore, Applicants have concluded that ATCC21430 is *Rhodococcus rhodochrous*.

In view of the above, Applicants respectfully submit that the recitation "ATCC21430 *Rhodococcus rhodochrous*" is taxonomically correct, and thus is definite and enabled.

(ii) As to the fact that ATCC21387 is recited as Brevibacterium sterolicum in the ATCC catalogue

Applicants respectfully submit that as shown on page 91 of Reference 1 (Catalogue of Strains I, Fifteen Edition (1982)), ATCC21387 is classified as *Brevibacterium sterolicum*, a strain which was deposited by Kyowa Hakko Kogyo Co., Ltd who is an assignor of this application.

Applicants have classified ATCC21387 as *Brevibacterium sterolicum* at the time of deposit to ATCC, and examined again various chemotaxonomical characteristics of the strain prior to the filing of this application. As a result, it has been found that ATCC21387 contains C26-C48 mycolic acid as a lipid component. However, as shown

in page 1267 of Reference 5 (Bergey's Manual of Systematic Bacteriology, volume 2, 1986 , a copy of which is attached herewith), the lipid components of microorganisms belonging to *Brevibacterium* do not contain mycolic acid. Therefore, it was considered that ATCC21387 belongs to genus other than *Brevibacterium*. On the other hand, various chemotaxonomical characteristics of ATCC21387 including lipid components were consistent with those of microorganisms belonging to *Rhodococcus*. Further, the DNA-DNA homology value with microorganisms belonging to *Rhodococcus* was examined, and as a result, it has been found that ATCC21387 showed a high value of 100% or more with ATCC6939 which is a Type strain of *Rhodococcus equi*. Thus, it has been concluded that ATCC21387 is *Rhodococcus equi*.

As mentioned above, it is taxonomically correct that ATCC21387 is *Rhodococcus equi*, and thus, the recitation "ATCC21387 *Rhodococcus equi*" recited in Claim 8 is definite and enabled.

(iii) As to the fact that ATCC19240 is recited as Brevibacterium thiogentalis in the ATCC catalogue

Applicants have examined various chemotaxonomical characteristics of ATCC19240 prior to the filing of this application. As a result, it has been found that ATCC19240 contain mycolic acid as lipid component. However, as shown in page 1267 of Reference 5 (Bergey's Manual of Systematic Bacteriology, volume 2, 1986), the lipid components of microorganisms belonging to *Brevibacterium* do not contain mycolic acid. Therefore, it was considered that ATCC19240 belongs to genus other than *Brevibacterium*. On the other hand, various chemotaxonomical characteristics of

ATCC19240 including lipid components were consistent with those of microorganisms belonging to *Corynebacterium*. Further, the DNA-DNA homology value with microorganisms belonging to *Corynebacterium* was examined, and as a result, it has been found that ATCC19240 showed a high value of 100% or more with ATCC9002 which is a Type strain of *Corynebacterium glutamicum*. Thus, it has been concluded that ATCC19240 is *Corynebacterium glutamicum*.

As mentioned above, it is taxonomically correct that ATCC19240 is *Corynebacterium glutamicum*, and thus the claimed ATCC19240 *Corynebacterium glutamicum* is definite and enabled.

(iv) As to the fact that ATCC7005 is recited as Corynebacterium hoagii in the ATCC catalogue

As shown in left column "b" of page 1275 of Reference 5 (Bergey's Manual of Systematic Bacteriology, volume 2, 1986), *Corynebacterium hoagii* ATCC7005 is identified to be the same species as *Rhodococcus equi* based on various chemotaxonomical characteristics. In Reference 5, an authority in microorganism classification, *Corynebacterium hoagii* ATCC7005 is classified as *Rhodococcus equi*.

As mentioned above, it is taxonomically correct that ATCC7005 is *Rhodococcus equi*, and thus this recitation is definite and enabled.

(v) As to the fact that ATCC15921 is recited as Brevibacterium lyticum in the ATCC catalogue

As shown in right column, pages 48-51 of Reference 5 (Bergey's Manual of Systematic Bacteriology, volume 2, 1986), *Brevibacterium lyticum* is identified to be the same species as *Cellulomonas cellulans* based on various chemotaxonomical characteristics. As present, the name of "*Brevibacterium lyticum*" is not used in the taxonomy, and "*Brevibacterium lyticum*" is standardized into "*Cellulomonas cellulans*".

As mentioned above, it is taxonomically correct that ATCC15921 is *Cellulomonas cellulans*, and thus this recitation is definite enabled.

In view of the above, Applicants respectfully submit that the rejection of Claims 7-9 under 35 U.S.C. § 112, first and second paragraphs have been overcome by the amendment of these claims. Accordingly, it is respectfully requested that this rejection be reconsidered and withdrawn.

Rejection of Claim 8 under 35 U.S.C. § 112

Claim 8 is rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which allegedly was not sufficiently described in the specification to be enabled thereby. In particular, the Examiner inquires about the designations "JCM", "IFM" and "IFO" recited in Claim 8 and requests a declaration to the effect that the corresponding strains were publicly available at the time of the invention.

Applicants respectfully submit that the recitation "*Gordona rubropertinctus*" has been canceled in Claim 7, and the recitation "*Gordona rubropertinctus* IFM-33" has been

canceled in Claim 9. Accordingly, Applicants respectfully submit that this rejection has been overcome.

Applicants respectfully submitted References 6 and 7 (Institution for Fermentation Osaka (IFO); and Japan Collection of Microorganisms RIKEN (The Institute of Physical and Chemical Research) respectively. References 6 and 7 are copies of website where disclosing that IFO and JCM (Japan Collection of Microorganisms) are official microorganism deposit authorities and the strains of IFO numbers or JCM numbers recited in Claim 8. The strains recited in Claim 8 will be given upon request by the IFO and JCM. Since the strain subdivision function of IFO has been transferred to Biological Resource Center (NRBC) of National Institute of Technology and Evaluation (NITE), a copy of website of NRBC is also enclosed with Reference 6 , a copy of which is attached herewith.

Rejection of Claims 1-9 under 35 U.S.C. § 112, second paragraph

Claims 1-9 are rejected under 35 U.S.C. § 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the invention. In this regard, the Examiner notes that Claim 1 recites that the cultured microorganism does not show hyphal growth and alleges that in contrast, the genera, species and strains recited in Claims 6-9 which all depend from Claim 1, do show hyphal growth to at least some extent. In particular, the Examiner asserts that with one exception (*Shingomonas*), all of the genera recited in Claims 6-9 belong to the *Actinomycetes*, the latter being acknowledged at page 2, last paragraph, of the present application to "grow with

filamentous forms by elongating hyphae". Additionally, the rejection alleges that the expression "treated cells" in Claim 5 is redundant.

Applicants respectfully submit that Claims 1, 5, and 6 have been amended to overcome this rejection. Specifically, Claims 1 and 6 have been amended to clearly recite microorganism having no ability to sporulate and showing no hyphal growth in a culture broth. Claim 5 has been amended to remove the redundant recitation "treat cells".

Applicants respectfully submit that as shown in Table 26.3 on page 2354 of Reference 4 ((Bergey's Manual of Systematic Bacteriology, volume 4, 1989), it is a scientific fact that all of microorganisms belonging to *Actinomysetes* do not always grow with filamentous forms by elongating hyphae.

As is clear from the description at page 2 of the present specification: filamentous fungi and *Actinomycetes* having an activity of producing the compound (VI-a) or (VI-b) from a compound (V-a) or (V-b) grow with filamentous form by elongating hyphae in a fermenter, the filamentous fungi and *Actinomysetes* described above grow with filamentous form by elongating hyphae in a culture broth. Therefore, as recited at line 13 of page 2 to line 4 of page 3 of the present specification, some problems occur in culture solution and hydroxylation reaction. Further, since the filamentous fungi and *Actinomysetes* form spores, contamination problem occurs in culture and purification processes (see second paragraph of page 3 of the present specification).

As recited at lines 14-21 of page 3 of the specification, an object of the present invention is to produce compound (VI-a) or (VI-b) by hydroxylation of compound (V-a) or (V-b) using a microorganism having no sporulability and showing no hyphal growth.

The present inventors have discovered that some microorganisms having no sporulability and showing no hyphal growth in culture broth, such as *Mycobacterium*, *Corynebacterium*, *Brevibacterium*, *Rhodococcus*, *Gordonia*, *Arthrobacter*, *Micrococcus*, *Cellulomonas* and *Sphingomonas*, specifically microorganisms belonging to the species recited in the amended Claim 7, more specifically the strains recited in the amended Claims 8 and 9, have an activity of producing compound (VI-a) or (VI-b) by hydroxylation of compound (V-a) or (V-b).

Therefore, the amendment of the specification and claims are within the original disclosure of this application and does not constitute new matter.

As discussed above, the microorganisms recited in the amended Claim 1 and the microorganisms belonging to the genus recited in Claim 6 are limited to hose having no sporulability and showing no hyphal growth in culture broth. The microorganisms of the species or the strains recited in Claims 7-9 are those having no sporulability and showing no hyphal growth in culture broth. Also, the amendment made to the specification at page 2 is consistent with the Amended Claims 1-9. Therefore, as amended, Claims 1-9 are definite. Accordingly, Applicants respectfully requested that the rejection mad under U.S.C. § 112 second paragraph be reconsidered and withdrawn.

Rejection of Claims 1-9 under 35 U.S.C. § 102(a) and 103(a)

Claims 1-9 are rejected under 35 U.S.C. § 102(a), as allegedly anticipated by or, in the alternative, under 35 U.S.C. § 103(a), as allegedly obvious over each of four documents, i.e.,

(a) WO 99/60151 to Kranjc et al. (corresponding to U.S. Patent No. 6,365,382);

(b) U.S. Patent No. 6,043,064 to Davis et al. (corresponding to Japanese Application No. 7-184670 acknowledged at page 2 of the present application);

(c) U.S. Patent 5,942,423 to Demain et al.; and

(d) Okazaki et al., J. Antibiot. 36: 1176-1183, 1983

in light of the ATCC website.

WO 99/60151 to Kranjc et al. (corresponding to U.S. Patent No. 6,365,382)

The Office Action states that Kranjc et al. teach a process of hydroxylation using a strain of *Amycolatopsis orientalis* ATCC19795. ATCC19795 was deposited as *Streptomyces orientalis*, and other strains of this species are or have been classified as *Norcardia orientalis*. Inasmuch as at least strain ATCC21430 is now classified as *Norcardia sp.* and in view of the inconsistencies and ambiguities in the instant record, it is stated that the process of the present invention is anticipated by the reference. Based on the website of the ATCC, some strains of *Nocardia* are now classified as *Amycolatopsis* and the like.

Further, the Office Action states that even if the claimed microorganism is not identical to the referenced microorganisms with regard to some unidentified characteristics, the differences are considered to be so slight that the referenced microorganisms is likely to possess the same characteristics of the claimed microorganism particularly in view of the similar characteristics which have been shown

to share. Thus, the rejection reasons that the claimed process would have been obvious those skilled in the art. Applicants respectfully traverse.

As mentioned in the above (2)(C)(i), it is clear that the taxonomically correct name of ATCC21430 is *Rhodococcus rhodochrous*. It is also clear that the taxonomically correct name of ATCC19795 is *Amycolatopsis orientalis*. The main menaquinone of ATCC21430 is MK-8 (H_2) as stated in the above (2)(C)(i), and the main menaquinone of microorganisms belonging to *Amycolatopsis* is MK-9 (H_2, H_4) as shown in page 2336 of Reference 4 (Bergey's Manual of Systematic Bacteriology, volume 4, 1989). Therefore, Applicants respectfully point out that ATCC21430 is not classified as *Amycolatopsis*.

In view of the above, it is clear that *Amycolatopsis orientalis* ATCC19795 of Kranjc et al. is completely different from *Rhodococcus rhodochrous* ATCC21430 used in the present invention. Also, *Amycolatopsis orientalis* ATCC19795 has sporulability as stated in page 4, line 31 of Kranjc et al.. In contrast, *Rhodococcus rhodochrous* ATCC21430 has no sporulability. Therefore, Kranjc et al. neither teach or suggest the claimed invention.

According to classification manuals known in the art, such as Bergey's Manual (References 4 and 5), the genus is classified according to various chemotaxonomical characteristics. Hence, it is common in the art to determine that DNA-DNA homology value of 20% or less between microorganisms belong to different genus based on various chemotaxonomical characteristics. It is clear that the microorganisms having a homology of only 20% or less on nucleotide sequence level of DNA cannot share similar property.

Therefore, there is no ground for the Examiner's comments that the hydroxylation reaction using microorganisms belonging to *Rhodococcus* is obvious from the disclosure of Kranjc et al. that microorganisms belonging to *Amycolatopsis* has an hydroxylation activity.

Accordingly, nothing in the Kranjc et al. document and/or the ATCC website teaches or suggests the claimed invention.

U.S. Patent No. 6,043,064 to Davis et al.

The Office Action states that Davis et al. teach a process of hydroxylation using a strain of *Amycolatopsis autotrophica* ATCC35024. ATCC35024 is now classified as *Pseudonocardia autotrophica*, but was deposited as *Nocardia autotrophica*. Inasmuch as at least strain ATCC21430 is now classified as *Norcardia sp.* and in view of the inconsistencies and ambiguities in the instant record, it is stated that the process of the present invention is anticipated by the reference. Based on the website of the ATCC, some strains of *Nocardia* are now classified as *Pseudonocardia* and the like.

Further, the Office Action states that even if the claimed microorganism is not identical to the referenced microorganisms with regard to some unidentified characteristics, the differences are considered to be so slight that the referenced microorganism is likely to possess the same characteristics of the claimed microorganism particularly in view of the similar characteristics which have been shown to share. Thus, the rejection reasons that the claimed process would have been obvious to those skilled in the art. Applicants respectfully traverse.

It is clear that the correct name of ATCC35024 is *Pseudonocardia autotrophica*. As shown in page 2336 of Reference 4 (Bergey's Manual of Systematic Bacteriology, volume 4, 1989), the main menaquinone of microorganisms belonging to *Pseudonocardia* is MK-8 (H_4). Therefore, as discussed in the previous section, it is clear that *Pseudonocardia autotrophica* ATCC35024 is completely different from *Rhodococcus rhodochrous* ATCC21430. Also, *Pseudonocardia autotrophica* ATCC35024 has sporulability as stated in left column, line 1 of page 2376 of Reference 4 (Bergey's Manual of Systematic Bacteriology, volume 4, 1989), but *Rhodococcus rhodochrous* ATCC21430 has no sporulability.

Further, taxonomically, *Pseudonocardia* is completely different from *Rhodococcus*. As discussed, it is clear that microorganisms belonging to *Pseudonocardia* are different from those belonging to *Rhodococcus* in its properties.

Accordingly, nothing in the Davis et al. document and/or the ATCC website teaches or discloses the claimed invention.

U.S. Patent 5,942,423 to Demain et al.

The Office Action states that Demain et al. teach a process of hydroxylation using a strain of *Actinomadura*. Inasmuch as at least strain ATCC21430 is now classified as *Norcardia sp.* and in view of the inconsistencies and ambiguities in the instant record, it is stated that the process of the present invention is anticipated by the reference. Based on the website of the ATCC, some strains of *Nocardia* are now classified as *Actinomadura* and the like.

Further, the Examiner mentions that even if the claimed microorganism is not identical to the referenced microorganisms with regard to some unidentified characteristics, the differences are considered to be so slight that the referenced microorganism is likely to possess the same characteristics of the claimed microorganism particularly in view of the similar characteristics which they have been shown to share. Thus, the claimed process would have been obvious to those skilled in the art.

As shown in left column, lines 14 and 15 of page 2511 of Reference 4 (Bergey's Manual of Systematic Bacteriology, volume 4, 1989), the main menaquinone of microorganisms belonging to *Actinomadura* is MK-9 (H_4) or MK-9 (H_6). Therefore, as mentioned in the above (i), it is clear that microorganisms belonging to *Actinomadura* recited in Demain et al. is completely different from *Rhodococcus rhodochrous* ATCC21430. Also, microorganisms belonging to *Actinomadura* have sporulability as stated in left column, lines 5-6 of page 2511 of Reference 4 (Bergey's Manual of Systematic Bacteriology, volume 4, 1989), but *Rhodococcus rhodochrous* ATCC21430 has no sporulability.

Further, taxonomically, *Actinomadura* is completely different from *Rhodococcus*. As mentioned in the above (i), it is clear that microorganisms belonging to *Actinomadura* are different from those belonging to *Rhodococcus* in its properties.

Accordingly, nothing in the Demain et al. document and/or the ATCC website teaches or suggests the claimed invention.

Okazaki et al., J. Antibiot. 36: 1176-1183, 1983

The Office Action states that Okazaki et al. teach a process of hydroxylation using a strain of *Nocardia*. Inasmuch as at least strain ATCC21430 is now classified as *Norcardia sp.* and in view of the inconsistencies and ambiguities in the instant record, it is stated that the process of the present invention is anticipated by the reference. Based on the website of the ATCC, some strains of *Nocardia* are now classified as *Rhodococcus* and the like.

Further, the Office Action states that even if the claimed microorganism is not identical to the referenced microorganisms with regard to some unidentified characteristics, the differences are considered to be so slight that the referenced microorganism is likely to possess the same characteristics of the claimed microorganism particularly in view of the similar characteristics which they have been shown to share. Hence the Examiner reasons that the claimed process would have been obvious to those skilled in the art. Applicants respectfully traverse.

As shown in page 2377 of Reference 4 (Bergey's Manual of Systematic Bacteriology, volume 4, 1989), the main menaquinone of microorganisms belonging to *Norcardia* is MK-8 (H_4) or MK-9 (H_2). Therefore, as mentioned in the above, it is clear that microorganisms belonging to *Nocardia* recited in Okazaki et al. is completely different from *Rhodococcus rhodochrous* ATCC21430.

Also, microorganisms belonging to *Norcardia* recited in Okazaki et al. belong to *Nocardia autotrophica*. Here, *Nocardia autotrophica* has sporulability as stated in "f" of

page 2362 of Reference 4 (Bergey's Manual of Systematic Bacteriology, volume 4, 1989), but *Rhodococcus rhodochrous* ATCC21430 has no sporulability.

Further, taxonomically, Nocardia is completely different from *Rhodococcus*. As mentioned in above (i), it is clear that microorganisms belonging to *Nocardia* are different from those belonging to *Rhodococcus* in its properties.

Accordingly, nothing in the Okazaki et al. document and/or the ATCC website teaches or suggests the claimed invention.

In view of the above, Applicants respectfully request that the Examiner reconsider and withdraw the foregoing rejections under 35 USC§§ 102 and 103.

Documents 1-7 cited above

In accordance with M.P.E.P.§ 609C(3), the documents cited above in support of Applicants' remarks are being submitted as evidence directed to an issue raised in the mentioned Official Action, and no additional fee or Certification pursuant to 37 C.F.R. §§ 1.97 and 1.98, or citation on a FORM PTO-1449 is believed to be necessary.

CONCLUSION

In view of the foregoing, it is believed that all of the claims in this application are in condition for allowance, which action is respectfully requested. If any issues yet remain which can be resolved by a telephone conference, the Examiner is respectfully invited to telephone the undersigned at the telephone number below.

Respectfully submitted,

Shin-ichi HASHIMOTO et al.

Bruce H. Bernstein
Reg. No. 29,027

31,226

February 9, 2004
GREENBLUM & BERNSTEIN, P.L.C.
1950 Roland Clarke Place
Reston, VA 20191
(703) 716-1191

P21252.A03

ATTACHMENT A. LISTING DOCUMENTS OF EVIDENCE

"Catalogue of Strains I: Fifteenth Edition, 1982", America Type Culture Collection, pp. 143, 380, 182, 183, and 159 (1982);

http://www.atcc.org/SearchCatalogs/longview.cfm?atccsearch=yes;

http://www.ifo.or.jp/index_e.html;

"Bergey's Manual of Systematic Bacteriology: Volume 4", Williams & Wilkins, pp. 2336, 2337, 2376, 2511, 2354, and 2361 (1989);

"Bergey's Manual of Systematic Bacteriology: Volume 2", Williams & Wilkins, pp. 1267, 1275, 1329 and 1274 (1986);

http://www.ifo.or.jp/index_e.html; and

http://www.jcm.riken.jp/JCM/aboutJCM.html